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COVID-19 Vaccine: A Way Out of Crisis

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Abstract

COVID-19 pandemic has taken toll on the entire globe at physical, emotional and administrative level; straining each and every aspect to its fullest. As on April 19/2021, COVID-19 has infected more than 140 million people around world with around 3 million deaths worldwide. Covid-19 vaccine has emerged as an important direction to walk the world out of this crisis. This chapter covers the basic aspects and principles of vaccination and Immunology and its application in COVID-19 pandemic. This chapter further covers the different type of vaccines being developed, their dosage schedule and route of administration, common adverse events and myths related to them.

Keywords: COVID-19, Pandemic, vaccine

1. Introduction

Immunization is a global health and development success story, saving millions of lives every year. Vaccines reduce risks of getting a disease by working with your body's natural defenses to build protection. When you get a vaccine, your immune system responds. Immunization is a key component of primary health care and an indisputable human right. It's also one of the best health investments money can buy. Vaccines are also critical to the prevention and control of infectious-disease outbreaks. They underpin global health security and will be a vital tool in the battle against antimicrobial resistance. The two terms vaccination and immunization has been used synonymously over the time but the two terms differ in their meaning [1].

"Vaccination" as per definition is defined as the process of administering the biochemical product referred to as vaccine in the human body whereas "Immunization" is defined as the process by which body develops immunity against the disease [2].

Vaccines train the immune system to develop antibodies and protect against the disease. As per World Health Organization (WHO) there are number of vaccines which had been developed against number of diseases namely Diphtheria, hepatitis B, measles, mumps, pertussis, polio and many more. On similar grounds, to tackle the menace of COVID-19, various vaccines have been developed [3].

2. Types of vaccines

Vaccines are of different types depending on the property of the pathogen/agent used in vaccine [4, 5].

a. On basis whether agent is live or killed.

- i. Live attenuated vaccine.
- ii. Inactivated vaccine.

b. On Basis whether part/entire agent used

- i. Whole cell vaccine.
- ii. Subunit vaccine.

c. On basis of Component of agent used.

- i. Nucleic acid based vaccines.
- ii. Protein based vaccines.
- iii. Polysaccharide vaccines.
- iv. Toxoid vaccines.
- v. Conjugate vaccines.

d. Newer type of vaccines

- i. Viral vector based vaccine.
- ii. Recombinant vaccines.

1. **Live attenuated vaccine:** These are the type of vaccines which contain weakened form of the pathogen. Immunogenicity of the pathogen is maintained while lowering the virulence and thus the disease-causing potential.
2. **Inactivated vaccine:** This type of vaccine contain pathogen in killed form. The pathogen is inactivated chemically or by other means thus removing the disease-causing potential of the vaccine. These vaccines are safer as compared to live attenuated vaccines as per the disease-causing potential of the vaccine.
3. **Whole cell vaccine:** In this type of vaccine agent is used in its complete form either live attenuated or killed.
4. **Subunit vaccine:** This type of vaccine uses a part of the agent rather than using the whole agent. This type of vaccine induces high and specific immune response as compared to other type of vaccines.

- 5. Nucleic acid-based vaccine:** These vaccines employ the genetic material as the active component of the vaccine. Based on the genetic material used, these can be either DNA based vaccine or RNA based vaccines. Further on the type of RNA used vaccines can be further divided into mRNA based and others. Most of the nucleic acid-based vaccines are of mRNA type.
- 6. Protein and polysaccharide-based vaccine:** These vaccines use the protein part and polysaccharide portion of the agent as active component respectively.
- 7. Toxoid vaccine:** Toxoid vaccines are special type of subunit vaccines in which the toxins produced by the disease-causing agent is chemically inactivated and the resulting toxoid is then used as active component of the vaccines. These

Sr.No.	Characteristics	Primary Immune Response	Secondary Immune Response
1	Definition	Primary Immune Response is the reaction of the immune system when it contacts an antigen for the first time.	Secondary Immune Response is the reaction of the immune system when it contacts an antigen for the second and subsequent times.
2	Appearance	Appears mainly in the lymph nodes and spleen.	Appears mainly in the bone marrow and then, in the spleen and lymph nodes.
3	Occurrence	This occurs in response to the primary contact of the antigen.	This occurs in response to the second and subsequent exposure to the same antigen.
4	Antibody Peak	The antibody level reaches its peak in 7–10 days.	The antibody level reaches its peak in 3–5 days.
5	Affinity of Antibody	Low affinity to their antigens.	High affinity to their antigens.
6	Responding Cells	Naive B cells and T cells	Memory B cells
7	Antibodies	Both thymus-dependent and thymus-independent antibodies are involved in the primary immune response.	Only thymus-dependent antibodies are involved in the secondary immune response.
8	Lag Phase	Long (4–7 days)	Short (1–4 days)
9	Types of Antibodies	A large amount of IgM and a small amount of IgG are produced during the primary immune response.	A large amount of IgG, a small amount of IgM are produced during the secondary immune response.
10	Amount of Antibody	Few antibodies are produced in the primary immune response.	100–1000 times more antibodies are produced in the secondary immune response.
11	Strength of the Response	The primary immune response is usually weaker than secondary immune response.	The secondary immune response is stronger.
12	Antibody level	Antibody level declines to the point where it may be undetectable.	The antibody level tends to remain high for longer time.

Table 1.
Differences between primary and secondary immune responses.

types of vaccines usually require booster doses after some interval to boost up the immune response.

8. **Conjugate vaccine:** This type of vaccines is subgroup under subunit vaccine. In these types of vaccines, a weaker antigen is combined with a stronger antigen in order to boost immune response for weaker antigen.

9. **Viral vector vaccine:** These vaccines use the modified version of different viruses as vector. Several different types of viruses have been used as vectors; adenoviruses being most commonly used [4].

3. Immunological response to vaccine

Immune response is divided into two types:

1. Primary immune response.
2. Secondary immune response.

The differences between these two have been described in **Table 1** [6].

4. Immunological responses to different type of COVID-19 vaccines

Inactivated vaccine: the genetic material is inactivated or destroyed in inactivated vaccine which after ingested by antigen presenting cell stimulate the helper T cells which in order stimulate B-cell to produce antibodies as described in **Figure 1** [7].

Example: COVAXIN (Bharat Biotech).

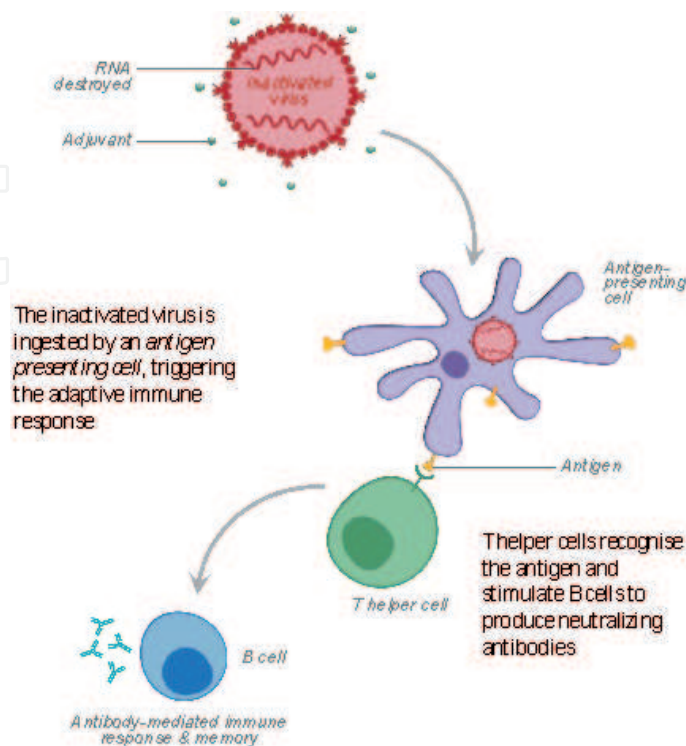


Figure 1.
Inactivated vaccine.

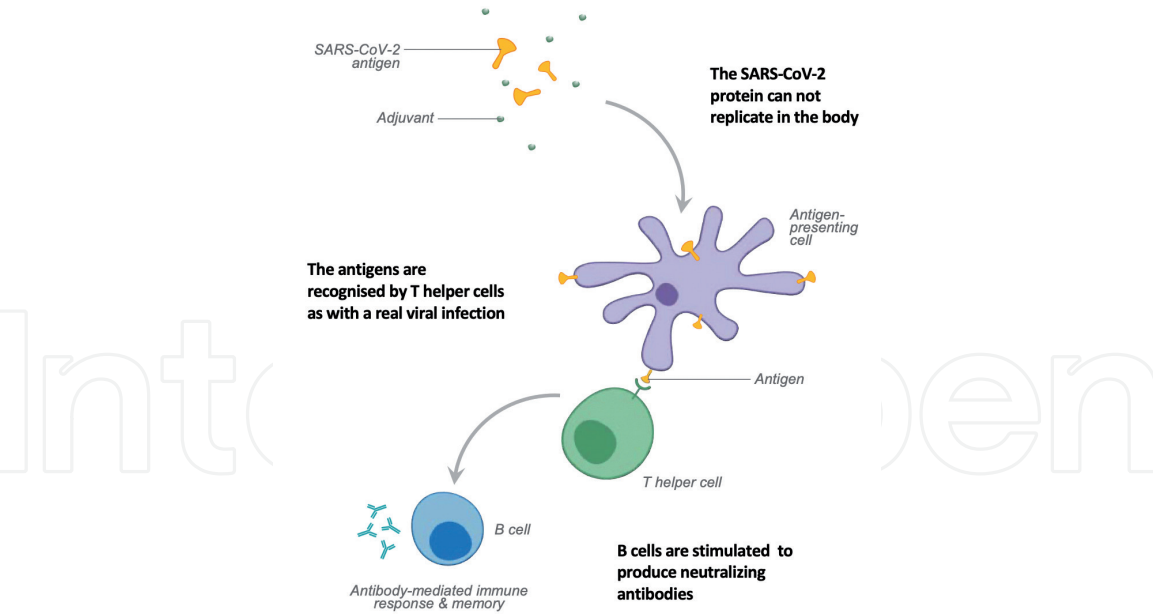


Figure 2.
Subunit vaccine.

Subunit Vaccine: In this vaccine only a part of the agent imitates like real infection and stimulate helper T cells which in turn stimulates B cells to produce antibodies as described in **Figure 2**.

Example: Novavax (protein subunit).

Viral vector Vaccine: these vaccines use non-coronavirus vector modified to carry gene coding for the SARS-COV-2 antigen. This antigen gets expressed on the cells infected gets ingested by antigen presenting cell which then project the complex to helper T cells which then activates both the B-Cells and Cytotoxic T cell as described in **Figure 3**.

Example: AstraZeneca-oxford vaccine and Sputnik-V (Gamaleya Research Institute).

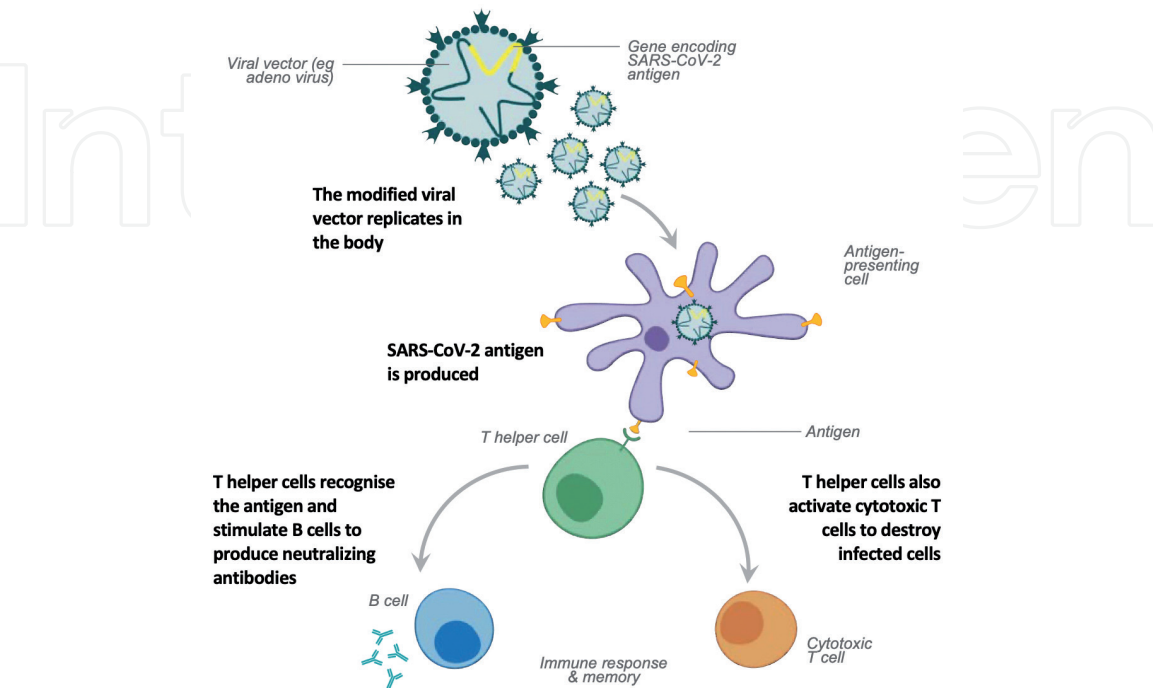


Figure 3.
Viral vector vaccine.

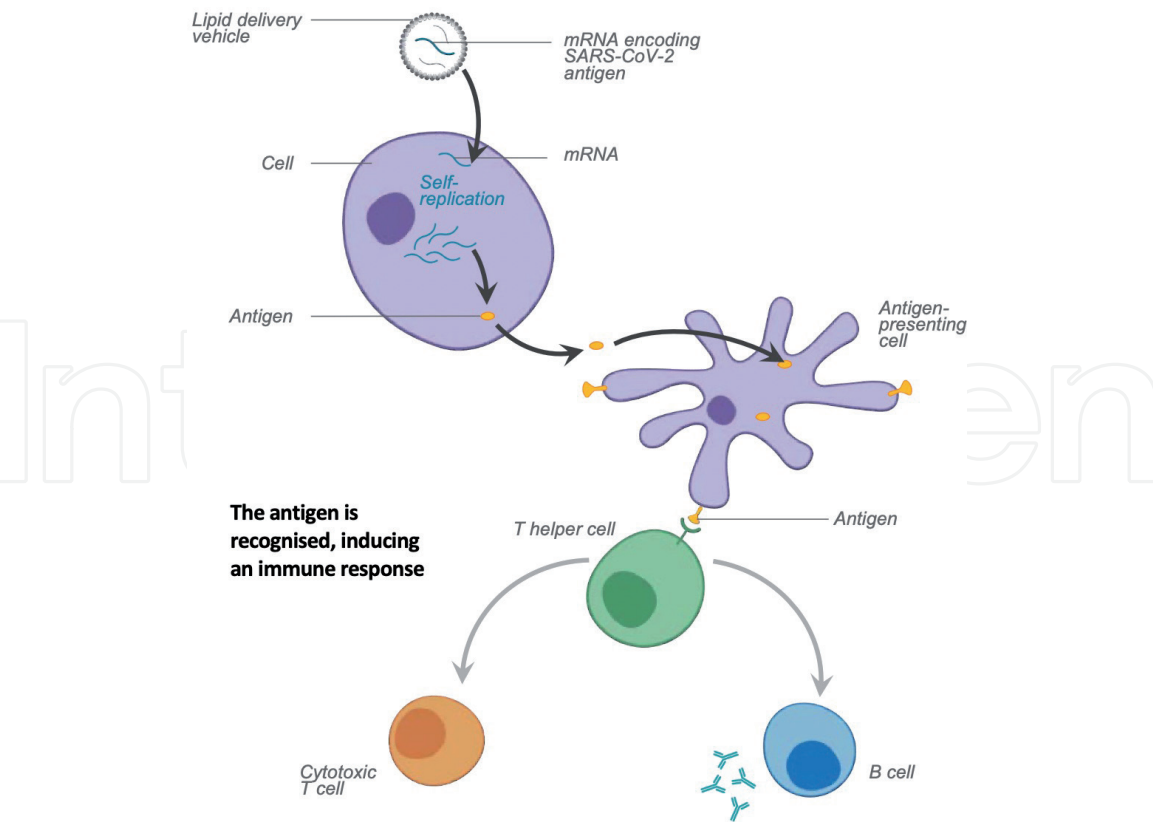


Figure 4.
RNA Vaccine

RNA Vaccine: RNA vaccines are antigen-coding strands of messenger RNA (mRNA) delivered inside a lipid coat. Once inside cells, the mRNA is translated into the protein antigen, which is secreted. The antigen is recognized, inducing an immune reaction. It induces T-helper and cytotoxic T-cells, and antibodies. mRNA also recognized by cells as ‘pathogen’ stimulating strong immune response as described in **Figure 4**.

Example: Pfizer/BioNTech and Moderna vaccine.

5. COVID-19 vaccines at glance

From February to June 2021, at least seven different vaccines across three platforms have been rolled out in countries [8–10]. Vulnerable populations in all countries are the highest priority for vaccination. At the same time, more than 200 additional vaccine candidates are in development, of which more than 60

Sr. No.	Name of vaccine/manufacturer	Type of vaccine	Age group	Efficacy
1.	Pfizer BioNTech	mRNA	Above 16 years	95.3%
2.	AstraZeneca	Viral vector	Above 18 years	63.09%
3.	Sputnik-V	Viral vector	Above 18 years	91.6%
4.	Moderna	mRNA	Above 18 years	94.1%
5.	Janssen/Johnson & Johnson	Viral vector	Above 18 years	66.3%
6.	Covaxin	Inactivated	Above 18 years	78%

Table 2.
Covid-19 vaccines rolled out in different countries for vaccination.

are in clinical development. COVAX is part of the ACT Accelerator, which WHO launched with partners in 2020. Some of the vaccines which have been rolled out are described in **Table 2**.

6. Dosage and schedule for vaccination

Most COVID-19 vaccines are designed for a two-dose schedule. Two dose vaccination works by mimicking natural immunity. After a first vaccine dose, the immune system needs time to generate a response and to create memory cells that will recognize the pathogen if it is encountered again. The person is considered immune from COVID-19 disease 14 days after the second dose of vaccine in two dose vaccine schedule. All these vaccines are administered Intramuscularly in the deltoid muscle as described in **Table 3**.

7. Vaccine storage and cold chain maintenance

Delivering vaccines to all corners of the world is a complex undertaking. It takes a chain of precisely coordinated events in temperature-controlled environments to store, manage and transport these life-saving products. This is called a cold chain. Vaccines must be continuously stored in a limited temperature range – from the time they are manufactured until the moment of vaccination. This is because temperatures that are too high or too low can cause the vaccine to lose its potency

Sr. No.	Name of vaccine	Dose	Dosage schedule	Route
1	Pfizer BioNTech	0.3 ml	0 + 21 days	Intra-muscular
2	AstraZeneca	0.5 ml	0 + 28 days (second dose can be taken as late as 8–12 weeks)	Intra-muscular
3	Sputnik-V	0.5 ml	0 + 21 days	Intra-muscular
4	Moderna	0.5 ml	0 + 28 days	Intra-muscular
5	Covaxin	0.5 ml	0 + 28 days	Intra-muscular
6	Janssen/Johnson & Johnson	0.5 ml	Single dose	Intra-muscular

Table 3.
Dosage schedule of COVID-19 vaccines.

COVID-19 vaccine	Storage temperature requirement
Pfizer BioNTech	-80 ⁰ c to -60 ⁰ c
AstraZeneca	+2 ⁰ c to +8 ⁰ c
Janssen/Johnson & Johnson	+2 ⁰ c to +8 ⁰ c
Sputnik-V	+2 ⁰ c to +8 ⁰ c (Dry form) -18.5 ⁰ c (Liquid form)
Moderna	+2 ⁰ c to +8 ⁰ c (for 30 days) -50 ⁰ c to -15 ⁰ c
Covaxin	+2 ⁰ c to +8 ⁰ c

Table 4.
Cold chain temperature requirements for COVID-19 vaccine.

(its ability to protect against disease). Once a vaccine loses its potency, it cannot be regained or restored. This cold chain temperature differs for different vaccines. Any fault in the cold chain maintenance could lead to wastage of vaccine. Storage condition requirements for various type of vaccines are described in **Table 4**.

8. Adverse effects and contraindications of COVID-19 vaccine

Vaccination is the process of administering foreign agent in the body which is usually associated with various adverse effects which are mostly of mild intensity but may cause severe adverse events in some [11].

Some of the known adverse events following immunizations are fever, pain and swelling at injection site, fatigue, chills, and headache. Some of the vaccine recipients may experience some severe adverse events like Anaphylactic reaction but the incidence of this is rare.

Contraindication to COVID-19 vaccine include severe allergic/anaphylactic reaction to any ingredient of the vaccine or to the first dose of vaccine. COVID-19 vaccine is also contraindicated in pregnant women or those suspected to be pregnant due to paucity of data in this group.

9. Myths related to COVID-19 vaccine

Myths preventing people from taking the vaccine are many and will be mentioned in another chapter, however one of these is:


COVID-19 vaccine was thought to cause infertility in women due to the resemblance of spike protein to the protein syncytin secreted by placenta. This was proved to be myth as the two protein have large difference in amino acid sequences hence ruling out the concern of infertility.

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